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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,115	12/06/2001	Hiroyuki Asako	7372-72249	3895
22242	7590	11/19/2003	EXAMINER	
FITCH EVEN TABIN AND FLANNERY 120 SOUTH LA SALLE STREET SUITE 1600 CHICAGO, IL 60603-3406			SLOBODYANSKY, ELIZABETH	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

KC

Office Action Summary	Application No.	Applicant(s)	
	10/004,115	ASAKO ET AL.	
	Examiner Elizabeth Slobodyansky	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 15 August 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 15-38 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-14 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received. 88
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 - 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 - 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4/8/03,
1/22/03; 10/17/02; 5/21/02; 3/21/02
- 4) Interview Summary (PTO-413) Paper No(s) _____.
5) Notice of Informal Patent Application (PTO-152)
 - 6) Other: _____

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DETAILED ACTION

Claims 1-38 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-14, in Paper filed August 15, 2003 is acknowledged. The traversal is on the ground(s) that "The statute requires independent and distinct, and the Requirement merely refers to "distinct", wherefore the Restriction should be reconsidered" (Remarks, 2nd paragraph). This is not found persuasive because "the law has long been established that dependent inventions ... may be properly divided if they are, in fact, "distinct" inventions, even though dependent" (MPEP 802.01).

This is not found persuasive because while 35 § U.S.C. 121 states that restriction may be required between independent and distinct inventions as delineated in MPEP 802.01 this language was intended to codify the existing practice of division at the time of the 1952 Patent Act which unquestionably included the division of dependent (or related) inventions. As such restriction is proper if two or more claimed inventions are either independent or distinct. see MPEP 803. Furthermore coexamination of each of the both groups would require search of subclasses unnecessary for the examination of the elected claims. For example, the search for the invention of Group II would include search of subclasses 435/183, 189, while the

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search for the invention of Group I would include search of at least subclasses 435/252.3, 320.1, 325; 536/23.2. Therefore, coexamination of each of these additional inventions would require a serious additional burden of search. Additionally, "Applicants also submit that the underlying assumption to the Restriction should also be reconsidered. Here, applicants have filed an IDS on April 8, 2003, and an IDS on January 22, 2003. The present Examiner has the EPO search report (see January 22, 2003 IDS) from which it is clear another examining authority has been able to review prior art as to all claims. Therefore, since the search has been done by another examining authority, Applicants request reconsideration and withdrawal of the Restriction consistent with the MPEP Section 803 ("if the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits ...")" (Remarks, 3rd paragraph). Applicants are reminded that this application is not a PCT application, nor is it a national stage application of a PCT application, and PCT practice with respect to lack of unity does not apply to this application.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups II-VII, there being no allowable generic

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or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed August 15, 2003.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claims 3-7, 12 and 13 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). In the interests of the compact prosecution, the claims have been treated as if they were properly written.

Claims 1-14 are objected to because of the following.

Claim 1 recites "a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate", whereas dependent claims 9-14 in addition recite "an enzyme capable of converting oxidized β-nicotinamide-adenine dinucleotide phosphate into a reduced form" (emphasis added). In this case since both proteins are enzymes, it is suggested that applicants maintain

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consistency through out the claims and refer to "an enzyme" instead of "a protein" in claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-14 recite "a polynucleotide coding for an enzyme capable of converting oxidized β-nicotinamide-adenine dinucleotide phosphate into a reduced form". The genus of polynucleotides coding for enzymes capable of converting oxidized β-nicotinamide-adenine dinucleotide phosphate into a reduced form is enormous and comprises structurally and functionally different enzymes from any source and man made. Claim 10 limits said enzymes to a glucose dehydrogenase. The genus of glucose dehydrogenase comprises enzymes that are NADP dependent and NADP independent. Even the former group comprises enzymes with different structures and substrates and stereo specificities.

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The specification discloses only a single species of the claimed genus, a DNA encoding glucose dehydrogenase from *Bacillus megaterium* IFO12108. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the “functionality” of “coding for enzymes capable of converting oxidized β-nicotinamide-adenine dinucleotide phosphate into a reduced form” or “glucose dehydrogenase” and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide coding for SEQ ID NO:1, including SEQ ID NO:2, does not reasonably provide enablement for a polynucleotide that hybridizes to a polynucleotide coding for SEQ ID NO:1 under stringent conditions and coding for a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate, said polynucleotide having an unknown homology to SEQ ID NO:2. The specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

The scope of claim 1(b) and claims 2-14, dependent thereon, is not commensurate with the enablement provided by the disclosure with regard to the indefinite number of polynucleotides encoding extremely large number of enzymes with different strictures encompassed by the claims.

The specification teaches a polynucleotide of SEQ ID NO:2 coding for a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate from *Penicillium citrinum* IFO4631 having the amino

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acid sequence of SEQ ID NO:1. The specification does not provide information regarding other combinations of substitute amino acids that would result in a mutant protein with the requisite enzymatic activity. While there is a great number of possible mutants, it is *a priori* unpredictable as to which mutant will exhibit the claimed activity. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of what changes in the amino acid sequence can be tolerated and result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of peptide mutants where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass polynucleotides of an unknown identity to SEQ ID NO:2 coding for a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the requisite activity; (B) the general tolerance of a protein capable of preferentially producing (S)-4-

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bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues of a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Therefore, one of ordinary skill would require guidance, such as information regarding the specific amino acid changes that can be made without impairing a protein of SEQ ID NO:1 enzymatic activity and/or changes that would render said activity, in order to make a polynucleotide coding for a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate having the sequence other than SEQ ID NO:2 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1(b) recites "stringent conditions". Said conditions can vary in different experimental settings. Without knowing the exact hybridization conditions, it is impossible to know polynucleotides of which structures hybridize.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. A polynucleotide of SEQ ID NO:2 encoding a protein capable of preferentially producing (S)-4-bromo-3-hydroxy butanoate by asymmetrically reducing 4-bromo-3-oxobutanoate of SEQ ID NO:1 naturally occurs in *Penicillium citrinum*.

As the products of Nature, it is unpatentable. Amending claim 1 to recite, for example, " an isolated polynucleotide" is suggested.

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Conclusion

The art made of record and not relied upon is considered pertinent to applicant's disclosure. EP 1 213 354 A3 (form PTO-1449 filed April 8, 2003) is a European counterpart of the instant invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD
Primary Examiner

November 13, 2003